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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,996	10/17/2003	Lothar Steidler	2676-6096US	1934

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EXAMINER	
SLOBODYANSKY, ELIZABETH	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,996	STEIDLER, LOTHAR	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11 and 18-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed March 30, 2006 amending claim 18 has been entered.

Claims 1-20 are pending.

Election/Restrictions

Claims 11 and 18-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group II, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 30, 2006.

Applicant's election without traverse of Group I, claims 1-10 and 12-17, in the reply filed on March 30, 2006 is acknowledged.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications filed in Europe on May 3, 2001 and December 7, 2001, respectively. It is noted, however, that applicant has not filed certified copies of the European applications as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to an isolated strain of *Lactococcus* species comprising a defective thymidylate synthase gene. Claims 2-4 depend from claim 1. Claims 3 and 4 limit the *Lactococcus* species to *Lactococcus lactis*. Claim 5 is drawn to a transformed strain of *Lactococcus* species comprising a defective thymidylate synthase gene. Claims 6-10 depend from claim 5. Claims 8 and 9 limit the *Lactococcus* species to *Lactococcus lactis*. Claim 12 is drawn to a composition comprising a transformed strain of *Lactococcus* species comprising a defective thymidylate synthase gene. Claims 13-17 depend from claim 12. Claims 15 and 16 limit the *Lactococcus* species to *Lactococcus lactis*. Therefore the claims recite the genus of *Lactococcus* species comprising a defective thymidylate synthase gene, said *Lactococcus* species comprising both naturally occurring defects in thymidylate synthase gene and defects caused by molecular biological techniques. Furthermore, the genus of *Lactococcus* species is diverse genus that encompassing thymidylate synthase gene or genes from any species of *Lactococcus*, including the subgenus of thymidylate synthase gene(s) from any subspecies of *L. lactis*.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical

species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification the genus of the genes of *Lactococcus* thymidylate synthase gene(s), including the subgenus of *L. lactis* thymidylate synthase gene(s), is represented by a single thymidylate synthase from *L. lactis* subsp. *lactis* that is disrupted by a functional human interleukin-10 expression cassette. The specification fails to describe any other representative species *Lactococcus* thymidylate synthase gene(s) by any identifying characteristics or properties other than the functionality of being *Lactococcus* thymidylate synthase gene(s).

The specification fails to define those structural features of *Lactococcus* thymidylate synthase gene(s) that are commonly possessed by members of the genus that distinguish them from others. The specification fails to provide the structure and function correlation common to all members of the genus of *Lactococcus* thymidylate

synthase gene(s). Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus.

Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention at the time of filing.

Claims 1-10 and 12-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *Lactococcus* strain comprising a disrupted thymidylate synthase gene, said gene comprising SEQ ID NOs: 3 and 5, does not reasonably provide enablement for a *Lactococcus* strain comprising a disrupted thymidylate synthase gene having an undefined percent identity to SEQ ID NOs: 3 and 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claim which encompasses comprising a disrupted thymidylate synthase gene from any *Lactococcus* strain having no known identity to SEQ ID NOs:3 and 5. The specification does not teach thymidylate synthase genes from other species of *Lactococcus* including other *subspecies of L. lactis*. While recombinant hybridization techniques are known, only highly homologous sequences can be identified using a given nucleic acid sequence. The state of the art provides no reasonable expectation of success in obtaining nucleic acid encoding a thymidylate synthase gene having an unknown identity to SEQ ID NOs: 3 and 5 and the result of such screening is unpredictable.

Without sufficient guidance, beyond that provided, disruption of thymidylate synthase genes of an unknown structure is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-10 and 12-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5, with dependent claims 6-10, and claim 12 , with dependent claims 13-17, are confusing because the connection between a defective thymidylate synthase gene and a transforming plasmid is unclear as reciting

Furthermore, claim 5 and 12 recite "said transforming plasmid not having an intact thymidylate synthase gene". Such definition of the plasmid is confusing as it defines it by what said plasmid is not instead of defining what it is.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steidler et al. in view of Taylor et al.

Steidler et al. (from PTO-1449 filed 10/17/03) teach a transformed *L. lactis* strain which secretes active murine interleukin-10 that is used to treat murine colitis.

Taylor et al. (from PTO-1449 filed 10/17/03) teach the disruption of the thymidylate synthase gene in *Saccharomyces cerevisiae* (see abstract and page 5302, right column, last paragraph to page 5303, left column, 1st paragraph). They teach that the disruption of said thymidylate synthase by inserting a 2.2 kb fragment of LEU2 gene.

They further teach that such disruption results in dependence on dTMP for growth. They teach that thymidylate synthase genes from various organisms show similar properties t the functional level (page 5304, left column, 2nd paragraph- right column, 1st paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a *L. lactis* strain which comprising a disrupted thymidylate synthase. This would allow to use said strain for the delivery of a drug (molecule of interest) to a patient without contaminating the outside environment where thymidine/thymine is not present in amount sufficient for said strain to survive. One of such molecules of interest can be interleukin-10, importance of which is taught by Steidler et al. One of ordinary skill in the art would have a reasonable expectation of success because the disruption of genes in bacteria were widely and routinely performed at the time the invention was made.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Patent 6,746,671 (Steidler et al.) is issued on application 09/838,718 that is identified by Applicant in IDS of 10/17/03.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

May 29, 2006